

Human A4 Receptor

1 TTGAGCCGGCAGACTGCGAAAAGTAGCTGGAGCCGGAGCAGGACAGAAACCTGTTGCTGCAGACGGGCTTGGTGGATTCTGGTTCCCTGCCCGACAGGGCTCGCCGGGAGAGGTTTCATC 120

121 ATGAATGAGAAATGGGACACAAAACCTCTTCAGAAAACCTGGCATCCCATCTTGGAAATGTCAATGACACAAAGCATCATCTGTACTCAGATATTAAATATTACCTATATGTGAACCTACTATCTTCAC 240

1 MN EKWD TNSSSE NWHP IWNVN DTKHHL YSD I N I T Y V N Y Y L H 40

241 CAGCCTCAAGTGGCAGCAATCTTTCATATTATTTCCCTACTTTCTGATCTTCTTTTGTGCAATGATGGGAAATACTGTGGTTTGTCTTTATTGTAATGAGGAACAAACATATGACACAGTCACT 360

41 QPV A A I F I I S Y F L I F F L C M M G N T V V C F I V M R N K H M H T V T 80

361 AATCTCTTCATCTTAAACCTGGCCATAAGTGATTACTAGTTGGCATATTCTGCAATGCCCTATAACACTGCTGGACAATATTATAGCAGGATGGCCATTTGGAAAACACCGATGTGCAAGATC 480

81 N L F I L N L A I S D L L V G I F C M P I T L L D N I I A G W P F G N T M C K I 120

481 AGTGGATTGGTCCAGGGAATATCTGTGCGAGCTTCAGTCTTTACGTTAGTTGCAATTGCTGTAGATAGGTTCCAGTGTGTGGTCTACCCCTTTTAAACCAAGCTCACTATCAAGACAGCG 600

121 S G L V Q G I S V A A S V F T L V A I A V D R F Q C V V Y P F K P K L T I K T A 160

601 TTTGTCAATTATGATCATCTGGTCTAGCCATCACCATTATGTCTCCATCTGCAGTAATGTTACATGTGCAAGAAATAATATACCGAGTGAGACTCAACTCCCAGAAATAAAACC 720

161 F V I I M I I W V L A I T I M S P S A V M L H V Q E E K Y Y R V R L N S Q N K T 200

721 AGTCCAGTCTACTGTGCCGGGAAGACTGGCCAAATCAGGAATGAGGAAGATCTACACCAGTGTGCTGTGTTGCCAACAATCTACCTGGCTCCCTCTCCCTCATGTGTCATGTATGGA 840

201 S P V Y W C R E D W P N Q E M R K I Y T T V L F A N I Y L A P L S L I V I M Y G 240

841 AGGATTGGAATTTCACTCTTTCAGGGCTGCAGTTCCTCACACAGGCAGGAAGAACCCAGGAGCAGTGGCACTGTGTTCCAGGAAGAAGCAGAGATCATTAAGATGCTCCTGATTTGTGGCC 960

241 R I G I S L F R A A V P H T G R K N Q E Q W H V V S R K K Q K I I K M L L I V A 280

961 CTGCTTTTATCTCTCATGGCTGCCCTGTGGACTCTAATGATGCTCTCAGACTACGCTGACCTTTCTCCAAATGAAGTGCAGATCATCAACATCTACATCTACCCCTTTTGCACACTGG 1080

281 L L F I L S W L P L W T L M M L S D Y A D L S P N E L Q I I N I Y I Y P F A H W 320

1081 CTGGCATTTCCGGCAACAGCAGTGTCAATCCCATCTTATGGTTTCTTCAACGAGAAATTTCCGCCGTGGTTTCCAAGAAGCTTTCCAGCTCCAGCTCTGCCAAAAGAGCAAAGCCTATG 1200

321 L A F G N S S V N P I I Y G F F N E N F R R G F Q E A F Q L Q L C Q K R A K P M 360

1201 GAAGCTTATACCCCTAAAAGCTAAAAGCCATGTGCTCATAAACACATCTAATCAGCTTGTCCAGGAATCTACATTTCAAAACCCCTCATGGGGAACCTTGTCTTTATAGGAAAAGTGTGAA 1320

361 E A Y T L K A K S H V L I N T S N Q L V Q E S T F Q N P H G E T L L Y R K S A E 400

1321 AAACCCCAACAGGAATTAGTGGAGAAATTAAAGAAACTACTAACAGCAGTGGATTTAAAGAGCTAGTGTGATAATCCCTAACTCTACTACGCATTATATATTTAAATCCATTGC 1440

401 K P Q Q E L V M E E L K E T T N S S E I * 421

- TM1 47-69
- TM2 82-104
- TM3 121-141
- TM4 160-182
- TM5 218-240
- TM6 275-297
- TM7 312-336

Figure 1

Amino Acid Homologies of A4 and Related Mammalian Receptors

Note: All sequences are human
Numbers below represent % similarity / % identity

A4	Orexin1	Orexin2	Y1	Y2	Y4	Y5	Gastrin	CCKA	NK1	Mu	
100	59/32	61/32	63/31	61/30	59/28	61/28	61/28	63/31	55/26	62/25	A4
	100	84/69	58/26	59/32	64/32	61/26	58/27	59/30	59/32	58/26	Orexin1
		100	60/27	60/31	63/32	59/26	61/29	58/29	56/31	58/28	Orexin2
			100	63/31	71/43	66/32	60/30	56/28	54/29	54/24	Y1
				100	62/33	63/32	56/27	56/29	59/30	57/24	Y2
					100	64/29	54/29	56/28	53/26	54/25	Y4
						100	58/28	55/26	57/24	61/26	Y5
							100	73/50	55/27	58/24	Gastrin
								100	57/30	55/26	CCKA
									100	60/26	NK1
										100	Mu

Legend:

Code:	GenBank Assession No.	Description
Orexin 1	AF041243	Human Orexin receptor-1
Orexin2	AF041245	Human Orexin receptor-2
Y1	P25929	Human Neuropeptide receptor Type1
Y2	P49146	Human Neuropeptide receptor Type2
Y4	P50391	Human Neuropeptide receptor Type4
Y5	U56079	Human Neuropeptide receptor Type5
Gastrin	P32239	Human Gastrin/Cholecystokinin Type B receptor
CCKA	P32238	Human Cholecystokinin Type A receptor
NK1	P25103	Human Neurokinin-1 / Substance-P receptor
Mu	P35372	Human Mu-type opioid receptor

Data above was obtained using the GAP program from the WISCONSIN PACKAGE Version 9.0

Parameters used: Symbol comparison table: oldpep.cmp *
Gap Creation Penalty: 30
Gap ExtensionPenalty: 1

* This is the default scoring matrix used by versions of the Wisconsin Package prior to Version 9.0. based on hte PAM250 table from M. Dayhoff¹.

1.) Schwartz, R. M. and Dayhoff, M. O. [1979]. Matrices for Detecting Distant Relationships. In *Atlas of Protein Sequence and Structure*, (M.O. Dayhoff, ed.), 5, Suppl. 3, (pp; 353-358), National Biomedical Research Foundation, Washington D.C., USA.

Figure 2

A4 vs. Human Y1 receptor

Percent Similarity: 63.032

Percent Identity: 30.585

1 MNEKWDTNSSSENWHPIWNV.NDTKHHLYSDINXTYVNYLHQPVAAIFI 49
 1MNSTLFSQVENHSVHSNFSEKNAQLLAFENDDDCHLPLAMI 40
 50 ISXFL....IFFLCMMGNTVVCFIVMRNKHMTVTNLFILNLAISDLLVG 95
 41 FTLALAYGAVIILGVSGNLALIIILKQKEMRNVNLTIVNLSFSDLLVA 90
 96 IFCMPITLLDNIIAGWPFNGTMCKISGLVQGISVAASVFTLVAVAVDRFQ 145
 91 IMCLPFTFVYTLMDHWVFGEAMCKLNPFVQCVSITVSIFSLVLIIVERHQ 140
 146 CVVYPFKPKLTIKTAFVIIMIIWVLAITIMSPSAVMLHVQEEKYYRVRLN 195
 141 LIINPRGWRPNNRHAYVGIAVIWVLAVASSLPFLIYQVMTDEPFQNVTLN 190
 196 SQNKTSPPVYWCREDWPNQEMRKIYTTVLFANIYLAFLSLIVIMYGRIGIS 245
 191 AYKDK...YVCFDQFSPDSHRLSYTTLLLVQLQYFGPLCFIFICYFKIYIR 237
 246 LFRAAVPHTGRKNQEQQWHVVSRRKKQKIIKMLLIVALLFILSWLPLWTLMM 295
 238 LKRRNNMMDKMRDNKYR...SSETKRINIMLLSIVVAFVAVCWLPPLTIFNT 284
 296 LSDYADLSPNELQIINIY....IYPFAHWLAFGNSSVNPPIYGFENENFR 341
 285 VFDWNH.....QIIATCNHNLFLCHLTAMISTCVNPIFYGFLNKNFQ 328
 342 RGFQEAFLQLCQKRAKPMAYTLKAKSHVLINTSNQLVQESTFQNPHE 391
 329 RDLQ..FFNFCDFRSRD.DDYETIAMSTMHTDVSKTSLK.....QAS 368
 392 TLLYRKSAEKPQQLVMEELKETTSSEI* 421
 369 PVAFKKINNNDNEKI*..... 385

Figure 3

[illegible]

Percent Similarity: 60.500
Percent Identity: 31.500

Top sequeunce: Human Orexin receptor-2
Bottom Sequeunce: Human A4 receptor

Figure 4

[illegible]

Percent Identity: 31.081

Figure 5

207020-0505001

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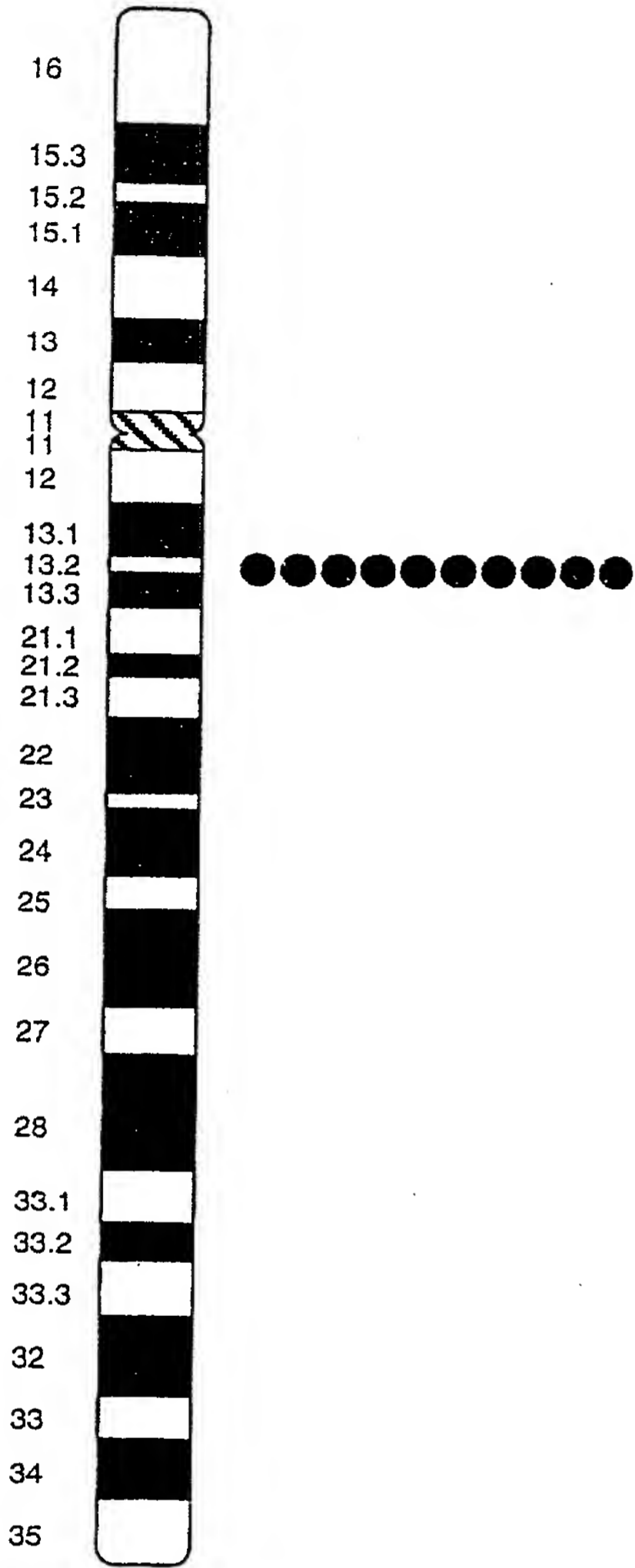


Figure 6